

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
20 November 2003 (20.11.2003)

PCT

(10) International Publication Number
WO 2003/094950 A3

(51) International Patent Classification⁷: **A61K 38/19**,
38/17, 38/07, 31/557, A61P 37/06, 29/00

(21) International Application Number:
PCT/EP2003/004872

(22) International Filing Date: 9 May 2003 (09.05.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
02010573.0 10 May 2002 (10.05.2002) EP
02011201.7 21 May 2002 (21.05.2002) EP
60/381,802 21 May 2002 (21.05.2002) US

(71) Applicant (for all designated States except US): **IPF PHARMACEUTICALS GMBH** [DE/DE]; Feodor-Lynen-Str. 31, 30625 Hannover (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FORSSMANN, Ulf** [DE/DE]; IPF PharmaCeuticals GmbH, Feodor-Lynen-Str. 31, 30625 Hannover (DE). **ELSNER, Jörn** [DE/DE]; Pickertsberg 35, D-31515 Wunstorf (DE). **ESCHER, Sylvia** [DE/DE]; Liebigstr. 6, D-30163 Hannover (DE). **SPODSBERG, Nikolaj** [DK/DE]; Rautenstr. 20, D-30171 Hannover (DE).

(74) Agents: **MEYERS, Hans-Wilhelm** et al.; Patent Attorneys, von Kreisler Selting Werner, P.O. Box 10 22 41, 50462 Köln (DE).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
26 February 2004

(15) Information about Correction:

Previous Correction:

see PCT Gazette No. 03/2004 of 15 January 2004, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A METHOD OF INHIBITING THE EMIGRATION OF CELLS FROM THE INTRAVASCULAR COMPARTMENT INTO TISSUES

(57) Abstract: A method of inhibiting the emigration of cells from the intravascular compartment into tissues (or through any membrane limiting any body compartment from another) by confronting the cells with an agonist specific for receptors involved with migration of said cells via a receptor thereby making the cell unresponsive to further activation.

WO 2003/094950 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/04872

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/19 A61K38/17 A61K38/07 A61K31/557 A61P37/06
A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, PAJ, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 167 527 A (EUROSCREEN S A ;NIEDERSAECHSISCHES INST FUER P (DE)) 2 January 2002 (2002-01-02) abstract	1-16
Y	paragraph '0015! paragraph '0041! paragraph '0061! claims 1-6,20-22 ----- -/--	1-16



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

8 October 2003

Date of mailing of the international search report

29. 12. 2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Lechner, O.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/04872

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DETHEUX M ET AL: "Natural proteolytic processing of hemofiltrate CC chemokine 1 generates a potent CC chemokine receptor (CCR)1 and CCR5 agonist with anti-HIV properties." THE JOURNAL OF EXPERIMENTAL MEDICINE. UNITED STATES 20 NOV 2000, vol. 192, no. 10, 20 November 2000 (2000-11-20), pages 1501-1508, XP002241991 ISSN: 0022-1007 the whole document</p>	1-16
Y	<p>MUENCH JAN ET AL: "Hemofiltrate CC chemokine 1(9-74) causes effective internalization of CCR5 and is a potent inhibitor of R5-tropic human immunodeficiency virus type 1 strains in primary T cells and macrophages." ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 46, no. 4, April 2002 (2002-04), pages 982-990, XP002241992 April, 2002 ISSN: 0066-4804 the whole document</p>	1-16
A	<p>TERAN L M: "CCL Chemokines and asthma" IMMUNOLOGY TODAY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 5, May 2000 (2000-05), pages 235-242, XP004198153 ISSN: 0167-5699 the whole document</p>	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/04872

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-10 (as far as relating to an in vivo method), 11 and 12 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-16 (only partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

claims 1-16 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-16 (only partially)

Present claims 1-6 and 13-15 relate to an extremely large number of possible compounds, partially defined by reference to a desirable characteristic or property, i.e. an agonist specific for receptors involved with migration of cells via a receptor thereby making the cell unresponsive to further activation, agonist used to inhibit the migration of the cells is a chemoattractant binding to a corresponding receptor or molecule binding to such a receptor, a chemokine, mutants and/or variants of the chemoattractant, an agonist specific for receptor involved with migration of blood circulating cells from the blood stream and chemo-attractant. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products/apparatus/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Claims 1-10 (as far as relating to in vivo methods of treatment), 11 and 13-16 relate to an extremely large number of ill defined pathologic conditions/diseases vaguely defined by reference to a result to be achieved/mechanism of action, i.e. inhibit the migration of the cells from the intravascular compartment into tissues, the cell is unresponsive to further activation for emigration to tissues, inhibit the migration of the cells, a disease state in mammals that is alleviated by treatment with a compound as claimed and a disease associated with migration of blood cells from the blood stream into tissues. This does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease). Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the diseases claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the use of R-CCL14'10-74! as defined in claims 7-10 for inhibiting the emigration of cells from the intravascular compartment into tissues (in vitro) and for treating inflammatory and other diseases (in vivo) mentioned on page 6, line 28- page 7, line 5 (benign prostatic hypertrophy).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-16 (all partially)

Use of R*-CCL14[10-74] in a method of inhibiting the emigration of cells from the intravascular compartment into tissues. R*...as defined in claims 7-10

2. Claims: 1-16 (all partially)

Use of R*-CXCL12[1-72] and functional variants thereof in a method of inhibiting the emigration of cells from the intravascular compartment into tissues. R*...as defined in claims 7-10

3. Claims: 1-6, 13-16 (all partially)

Use of a defensine in a method of inhibiting the emigration of cells from the intravascular compartment into tissues.

4. Claims: 1-6, 13-16 (all partially)

Use of a leukotriene in a method of inhibiting the emigration of cells from the intravascular compartment into tissues.

5. Claims: 1-6, 13-16 (all partially)

Use of a formyl-peptide in a method of inhibiting the emigration of cells from the intravascular compartment into tissues.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/04872

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1167527	A	02-01-2002	EP 1167527 A1	02-01-2002
			AU 1259501 A	08-05-2001
			WO 0131016 A2	03-05-2001
			CA 2387378 A1	03-05-2001
			EP 1224288 A2	24-07-2002
			JP 2003512843 T	08-04-2003
			US 2003158387 A1	21-08-2003
